Orale Antibiotika

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Agenda

- **Ganz kurz: Hintergrund**
- **Neues bzw. Kritisches zu Anwendung/klinische Studien (schwere Infektionen)**

Hintergrund – Oralisierung

- Teil des Deeskalations-Portfolios
- heute bei vielen Indikationen „studiert“, viele Studien allerdings mit Fluorchinolonen, in der Regel nur als „Sequenztherapie“
- kein Problem bei Substanzen mit guter bis sehr guter oraler Bioverfügbarkeit (und verlässlicher Compliance)
- bei ß-Lactamen und bestimmten Indikationen/Erregern in der Regel nicht empfohlen:
  - Meningitis/Hirnabszess
  - Endokarditis
  - Chronischen (Biofilm-)Infektionen

  } kritische Befunde & Stimmen
- ökonomisch interessant, bessere Lebensqualität

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Rose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.M. [illegible], M. Hopkins, J. Folb, H.E. Reynolds, E. [illegible], Marshall, N. [illegible], C.L. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

OVIVA

Early oral switch in low-risk *Staphylococcus aureus* bloodstream infection

Achim J. Kaasch, Luis Eduard López-Cortés, Jesús Rodríguez-Baño, José Miguel Cisneros, M. Dolores Navarro, Gerd Fätkenheuer, Norma Jung, Siegbert Rieg, Raphaël Lepeule, Laetitia Coutte, Louis Bernard, Adrien Lemaignen, Katrin Kösters, Colin R. MacKenzie, Alex Soriano, Stefan Hagel, Bruno Fantin, Matthieu Lafaurie, Jean-Philippe Talarmin, Aurélien Dinh, Thomas Guimard, David Boutoille, Tobias Welte, Stefan Reuter, Jan Kuytmans, María Luisa Martín, Emmanuel Forestier, Hartmut Stocker, Virginie Vitrat, Pierre Tattevin, Anna Rommerskirchen, Marion Noret, Anne Adams, Winfried V. Kern, Martin Hellmich, Harald Seifert, SABATO study group (members and affiliations listed in Acknowledgement record)

SABATO

medRxiv 2023.07.03.23291932; doi: https://doi.org/10.1101/2023.07.03.23291932

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Ekeing, M.D., Ph.D., Kare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høst[illegible], M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine S. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

POET

Home | About Me | Shorter Is Better | Oral Antibiotic RCTs | WikiGuidelines | Scientific Publications | Books | Laboratory

Osteomyelitis **Bacteremia** **Endocarditis** **cIAI** **cUTI**

Meta-Analysis Osteo, Bacteremia, Endocarditis

CLINICAL RESEARCH STUDY

Link to Systematic Review and Meta-Analysis (with forest plots)

THE AMERICAN JOURNAL of MEDICINE®

Oral Is the New IV. Challenging Decades of Blood and Bone Infection Dogma: A Systematic Review

Noah Wald-Dickler, MD,[a,b,c] Paul D. Holtom, MD,[a,b] Matthew C. Phillips, MD,[a] Robert M. Centor, MD,[d,e] Rachael. A. Lee, MD,[d,e] Rachel Baden, MD,[a] Brad Spellberg, MD[a]

[a]Los Angeles County + University of Southern California Medical Center, Los Angeles; [b]Department of Medicine, Keck School of Medicine, University of Southern California, Los Angeles; [c]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles; [d]Department of Medicine, University of Alabama at Birmingham School of Medicine, Birmingham; [e]Birmingham Veterans Affairs (VA) Medical Center, Birmingham, Ala.

https://www.bradspellberg.com/oral-antibiotics

Oral vs. IV Abx for Osteomyelitis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Greenberg	'87	30	Ciprofloxacin vs. std IV	50% (7/14) v 65% (11/16)
Gentry	'90	59	Ciprofloxacin vs. βL+aminoglyc	77% (24/31) v 79% (22/28)
Mader	'90	26	Ciproflox vs. βL/clinda+aminoglyc	79% (11/14) v 83% (10/12)
Gentry	'91	33	Ofloxacin vs. cephalosporin	74% (14/19) v 86% (12/14)
Gomis	'99	32	Ofloxacin vs. imipenem	69% (11/16) v 50% (8/16)
Schrenzel	'04	39	Fleroxacin+rifampin v βL/vanco	82% (18/22) v 65% (11/17)
Euba	'09	48	TMP-SMX+rifampin vs. cloxacillin	81% (17/21) v 77% (21/27)
Li	'19	1054	Std oral vs. std IV	87% (457/527) v 85% (450/527)
Manning	'22	60	PJI/DAIR: IV/Oral vs. IV only	71% (22/31) v 76% (22/29)
Total (N=9 RCTs)		1,381		84% (581/695) v 83% (567/686)

Success = absence of osteo at long term follow up (most studies >1 year); std = standard of care, protocol specified; all RCTs comparing oral to IV-only are in adults, however there are also 9 other adult and 8 pediatric RCTs or quasi-experimental studies comparing mostly oral vs. mostly oral, with high cure rates; refs at https://www.bradspellberg.com/oral-antibiotics

- 6 (sehr kleine) Studien mit Fluorchinolonen
- 1 große Studie (OVIVA)

https://www.bradspellberg.com/oral-antibiotics

OVIVA Trial

Li et al. NEJM 2019

Table S10: Overview of actual antibiotics (excluding rifampicin), as defined by agents used for more than one week during the initial six-week treatment period

	Participants randomized to IV Antibiotic* (N = 521)	Participants randomized to PO Antibiotic* (N = 523)	Total* (N = 1044)
Glycopeptides[a] (IV)	214 (41.1%)	22 (4.2%)	236 (22.6%)
Penicillins (IV)	38 (7.3%)	11 (2.1%)	49 (4.7%)
Cephalosporins (IV)	173 (33.2%)	8 (1.5%)	181 (17.3%)
Carbapenems (IV)	41 (7.9%)	5 (1.0%)	46 (4.4%)
Other single IV antibiotic	35 (6.7%)	2 (0.4%)	37 (3.5%)
Combination IV antibiotics	35 (6.7%)	6 (1.1%)	41 (3.9%)
Penicillins (PO)	8 (1.5%)	83 (15.9%)	91 (8.7%)
Quinolones[b] (PO)	33 (6.3%)	191 (36.5%)	224 (21.5%)
Tetracyclines[c] (PO)	4 (0.8%)	57 (10.9%)	61 (5.8%)
Macrolides / Lincosamide [d] (PO)	10 (1.9%)	68 (13.0%)	78 (7.5%)
Other single PO antibiotic (PO)	10 (1.9%)	54 (10.3%)	64 (6.1%)
Combination PO antibiotics (PO)	13 (2.5%)	87 (16.6%)	100 (9.6%)

The categories in this table were not mutually exclusive; 149 participants fell into more than one category and the data do not take account of adjunctive rifampicin which was analysed separately.

OVIVA Trial

Li et al. NEJM 2019

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[b] *Quinolones were ciprofloxacin in all but two cases, one each of moxifloxacin and levofloxacin. Of 191 participants in the oral arm who were prescribed quinolones, 160 (83.8%) were also prescribed rifampicin at some point during the trial.*

- 6 Studien mit Linezolid* (3 pädiatrisch)
- 4 Studien mit Fluorchinolonen

*Wilcox et al. Linezolid compared with teicoplanin for the treatment of suspected or proven Gram-positive infections. *JAC* 2004.

*Wilcox et al. Complicated skin and skin-structure infections and catheter-related bloodstream infections: noninferiority of linezolid in a phase 3 study. *CID* 2009.

Oral vs. IV Abx for Bacteremia

Author	Yr	N	Regimen (Oral vs. IV)	Success
Amodio-Groton	'96	50	Ciprofloxacin oral vs. IV—GNB	83% (20/24) v 77% (20/26)
San Pedro	'02	51	Linezolid vs. ceph—*S. pneumo*	93% (27/29) v 68% (15/22)
Deville	'03	36	Linezolid vs. vanco—GPC (peds)	80% (20/25) v 64% (7/11)
Jantausch	'03	103	Linezolid vs. vanco—GPC (peds)	72% (54/75) v 64% (18/28)
Kaplan	'03	80	Linezolid vs. vanco—GPC (peds)	82% (47/57) v 74% (17/23)
Schrenzel	'04	67	FQ + rif vs. βL/vanco—*Staph*	87% (34/39) v 89% (25/28)
Wilcox	'04	56	Linezolid vs. teicoplanin—GPC	89% (23/26) v 57% (17/30)
Wilcox	'09	166	Linezolid vs. vancomycin—GPC	75% (70/93) v 81% (59/73)
Monmaturopaj*	'12	17	Cefditoren vs. ceftriaxone—GNB	100% (6/6) v 91% (10/11)
Park	'14	59	Ciprofloxacin vs. std IV—GNB	93% (27/29) v 93% (28/30)
Omrani	'23	165	FQ/TMPSMX/BL vs. std IV—GNB	78% (65/83) v 74% (61/82)
Total (N=11 RCTs)		850		81% (393/486) v 76% (277/364)

*N = 82 pts with pyelonephritis of whom 17 were bacteremic with *E. coli*, patients were randomized to continue ceftriaxone or switch to oral ceftditoren at day 3. Refs at https://www.bradspellberg.com/oral-antibiotics

- 6 Studien mit Linezolid (3 pädiatrisch)
- 4 Studien[#] mit Fluorchinolonen

[#]Omrani et al. Switch to oral antibiotics in Gram-negative bacteraemia; a randomised, open-label, clinical Trial. *CMI* 2023.

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CMI CLINICAL MICROBIOLOGY AND INFECTION ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

ORIGINAL ARTICLE | ARTICLES IN PRESS

Switch to oral antibiotics in Gram-negative bacteraemia: a randomized, open-label, clinical trial

Ali S. Omrani • Sulieman H. Abujarir † • Fatma Ben Abid † • ... Wadha Alfouzan • Muna A. Almaslamani • SOAB Study Group †† • Show all authors • Show footnotes

Published: October 17, 2023 • DOI: https://doi.org/10.1016/j.cmi.2023.10.014

- 1476 Patienten gescreent, (nur) 174 randomisiert
- >60% Pyelonephritis/Urosepsis, >60% E.coli
- 4 Tage parenteral vorbehandelt
- Oralisierung: 30% Amoxi-Clav, 35% Oralceph, 19% Fluorchinolon, 16% Cotrimoxazol
- Ergebnisse ähnlich

Oral vs. IV Abx for Endocarditis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Stamboulian	'91	30	Amox 1 gm qid vs. CTX—*Strep*	100% (15/15) v 100% (15/15)
Heldman	'96	93	Cipro + Rif vs. std IV—*Staph*	95% (18/19) v 88% (22/25)
Iversen/ Bungaard[†]	'19	400	Std oral vs. std IV—GPC	74% (146/199) v 62% (125/201)
*Tissot-Dupont**	*'19*	*341*	*TMP-SMX+clinda vs. std IV--Staph*	*81% (138/171) v 70% (119/170)*
Totals (N=3 RCTs)	523			77% (179/233) v 70% (162/241)
(+ 1 quasi expt)*	*(864)*			*78% (317/404) v 68% (281/411)*

*Quasi-experimental, pre-post study. Italicized totals include the quasi-experimental data.
[†]Iversen reported early follow up, Bungaard 3 year follow up from the same study.
Refs at https://www.bradspellberg.com/oral-antibiotics

PLOS flags nearly 50 papers by controversial French COVID researcher for ethics concerns

December 13, 2022

In "expression of concern"

Controversial French researcher loses two papers for ethics approval issues

October 31, 2023

In "lack of IRB approval"

Hydroxychloroquine-COVID-19 study did not meet publishing society's "expected standard"

April 6, 2020

In "covid-19"

https://retractionwatch.com/2022/09/08/didier-raoult-papers-earn-expressions-of-concern-as-criminal-investigation-gets-underway/

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Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

- nur stabile Patienten mit klinischem Ansprechen nach mind. 10 Tagen intravenöser Therapie und ohne Indikation für operatives Vorgehen
- 2 orale Antibiotika (mit TDM !)
- „nur“ 20% (!) letztendlich in die Studie rekrutiert (davon waren 40% postoperativ)
- >50% Streptokokken

NEJM 2018

Table S2

Oral regimens recommended in the POET trial

Methicillin sensitive *Staphylococcus aureus* and coagulase-negative staphylococci

1) Dicloxacillin 1 g x 4 and fusidic acid 0.75 g x 2
2) Dicloxacillin 1 g x 4 and rifampicin 0.6 g x 2
3) Linezolid 0.6 g x 2 and fucidic acid 0.75g x 2
4) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2

Enterococcus faecalis:

1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2
2) Amoxicillin 1 g x 4 and moxifloxacin 0.4 g x 1
3) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2
4) Linezolid 0.6 g x 2 and moxifloxacin 0.4 g x 1

Streptococci with a minimal inhibitory concentration for penicillin of <1 mg/L:

1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2
2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2
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Iversen et al *NEJM* 2018

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3) Linezolid 0.6 g x 2 and fusidic acid 0.75 g x 2

Dicloxacillin 4 x 1 g
Amoxicillin 4 x 1 g

„Hochdosis“-Rifampicin
„Niedrigdosis“-Fusidinsäure

Iversen et al *NEJM* 2018

Streptococci

Amoxicillin and rifampicin	47 (52)
Amoxicillin and moxifloxacin	12 (13)
Rifampicin and linezolid	8 (9)
Moxifloxacin and linezolid	8 (9)
Amoxicillin and linezolid	7 (8)
Penicillin	3 (3)
Ampicillin and moxifloxacin	1 (1)
Ampicillin and rifampicin	1 (1)
Dicloxacillin and moxifloxacin	1 (1)
Moxifloxacin and clindamycin	1 (1)
Moxifloxacin and vancomycin	1 (1)





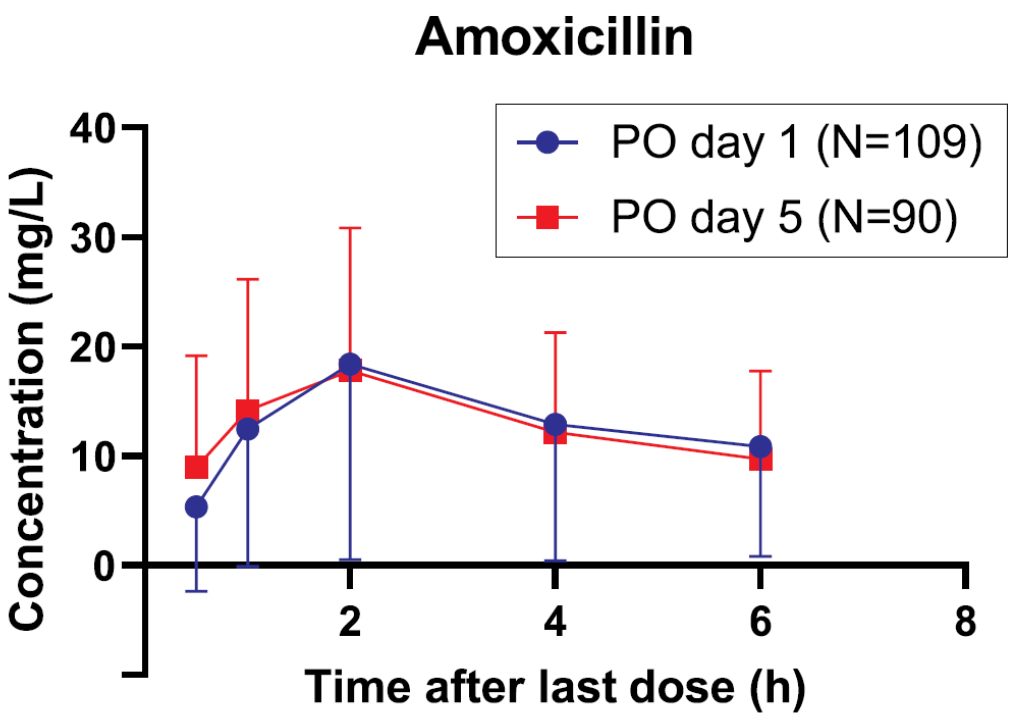

Clinical Infectious Diseases

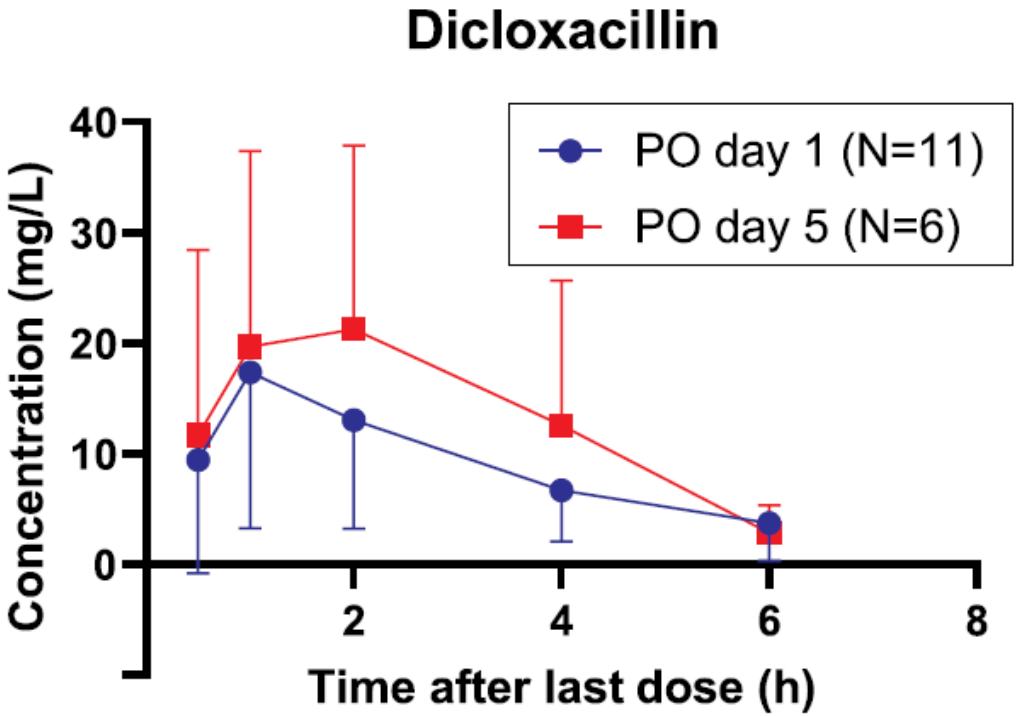
MAJOR ARTICLE

Attainment of Target Antibiotic Levels by Oral Treatment of Left-sided Infective Endocarditis: A POET Substudy

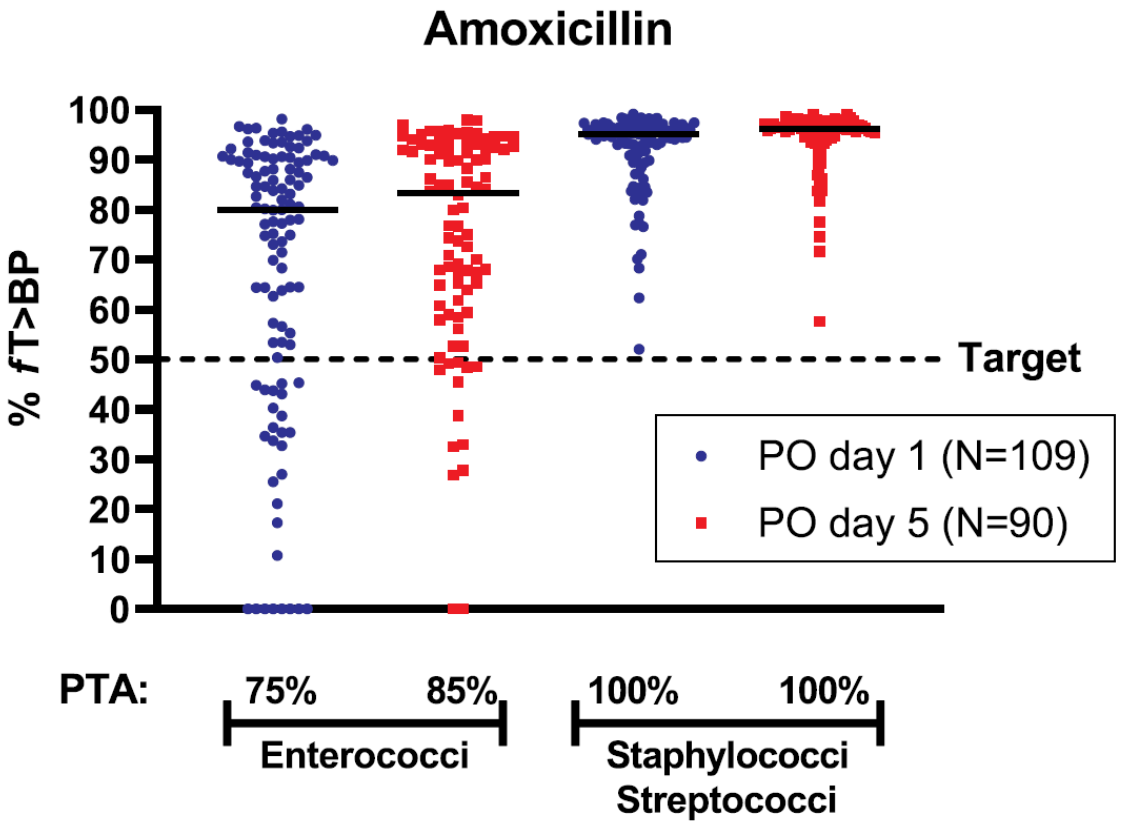
Magnus Bock,[1] Anna Marie Theut,[1] Johan G. C. van Hasselt,[2] Hengzhuang Wang,[1,3] Kurt Fuursted,[4] Niels Høiby,[1,3] Christian Johann Lerche,[1,5] Nikolaj Ihlemann,[6] Sabine Gill,[7] Ulrik Christiansen,[8] Hans Linde Nielsen,[9,10] Lars Lemming,[11] Hanne Elming,[12] Jonas A. Povlsen,[13] Niels Eske Bruun,[10,12,14] Dan Høfsten,[15] Emil L. Fosbøl,[15] Lars Køber,[14,15] Martin Schultz,[16] Mia M. Pries-Heje,[15] Jonas Henrik Kristensen,[17,18] Jens Jørgen Christensen,[14,19] Flemming S. Rosenvinge,[20,21] Christian Torp Pedersen,[22,23] Jannik Helweg-Larsen,[24] Niels Tønder,[22] Kasper Iversen,[14,18] Henning Bundgaard,[14,15] and Claus Moser[1,3]

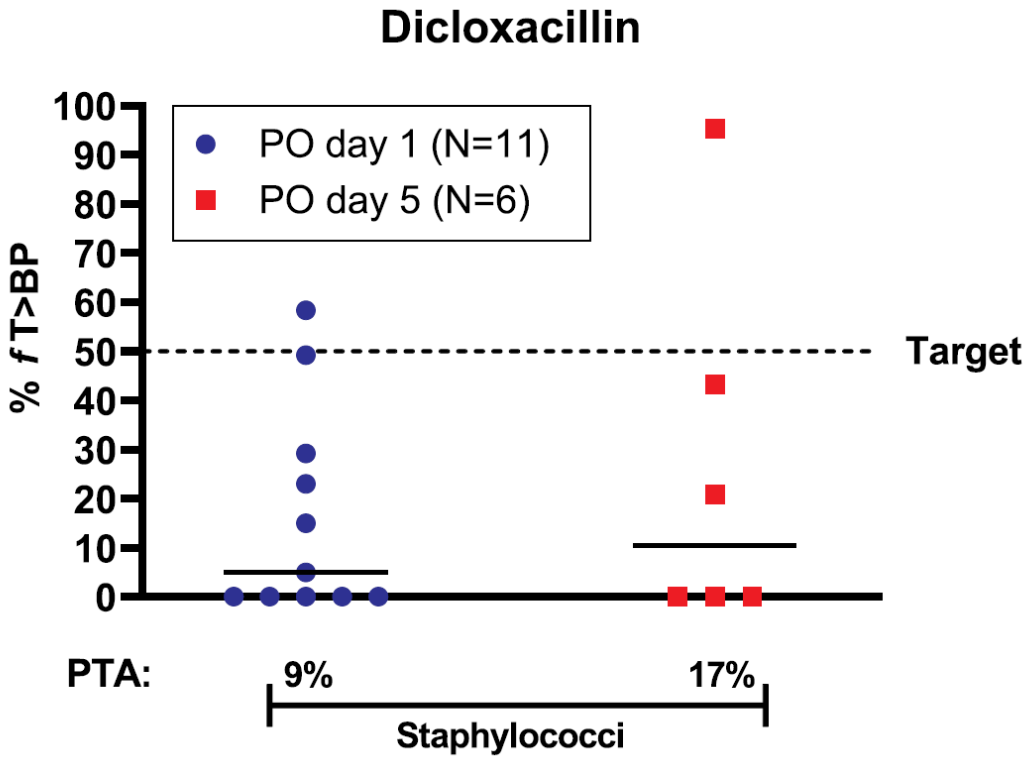
- N=236, darunter 175 mit zwei oralen Antibiotika
- TDM Tag 1 und 5, ~10% der Messungen unplausibel, sehr wenig Dicloxacillin
- Definition von Zielspiegeln (ß-Lactame: *f*T>MIC 50% bzw. *f*T>Grenzwert 50%)





Bock et al *CID* 2023





BP= **4 mg/L** **0.5 mg/L**

Bock et al *CID* 2023

Table 1. Clinical Breakpoints and Pharmacokinetic/Pharmacodynamic Targets

Drug	Dose	Approximate Unbound Fraction (%)	Bacterial Species	Clinical Breakpoint (mg/L)	Pharmacokinetic/ Pharmacodynamic Target
Amoxicillin	PO: 1000 mg q6 h	80	Enterococci	4	*f*T > BP or *f*T > MIC more than 50% of dosing interval[b]
			Staphylococci Streptococci	0.5[a]	
Dicloxacillin	PO: 1000 mg q6 h	3	Staphylococci	0.5[c]	*f*T >BP more than 50% of dosing interval[b]
	IV: 3000 mg q6 h				
Linezolid	PO or IV: 600 mg q12 h	Not used	Enterococci Staphylococci	4	AUC_{12}/BP >50 or AUC_{12}/MIC >50
			Streptococci	2[d]	
Moxifloxacin	PO or IV: 400 mg q24 h	50	Enterococci Streptococci	0.5[e]	*f*AUC_{24}/BP >30 or *f*AUC_{24}/MIC >30[b]
			Staphylococci	0.25	
Rifampicin[f]	PO: 600 mg q12 h	Not used	Staphylococci Streptococci	0.064	AUC_{12}/BP >500 or AUC_{12}/MIC >500

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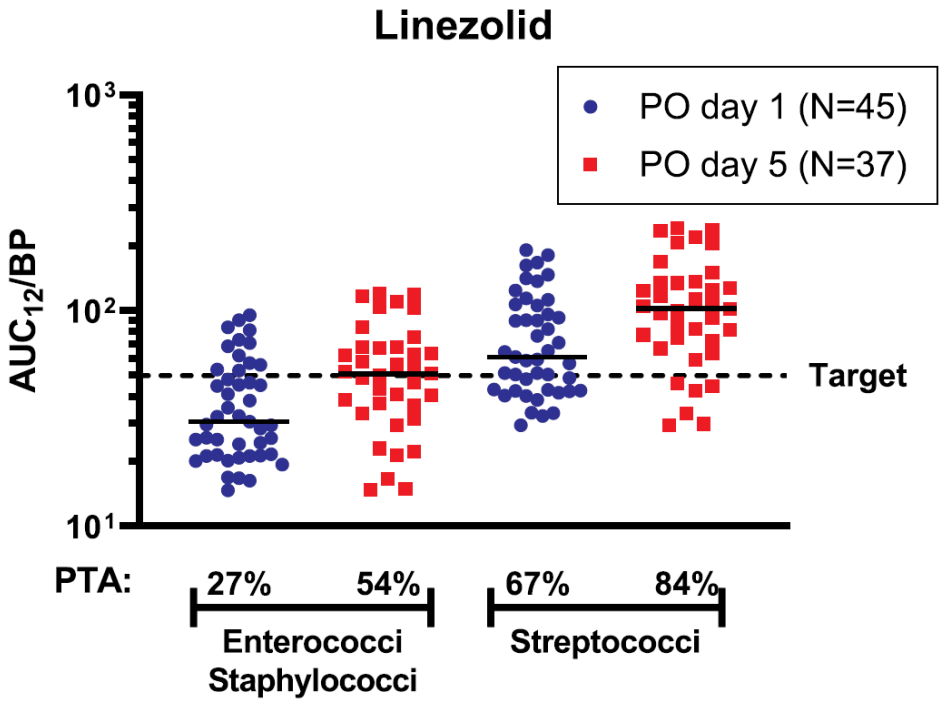

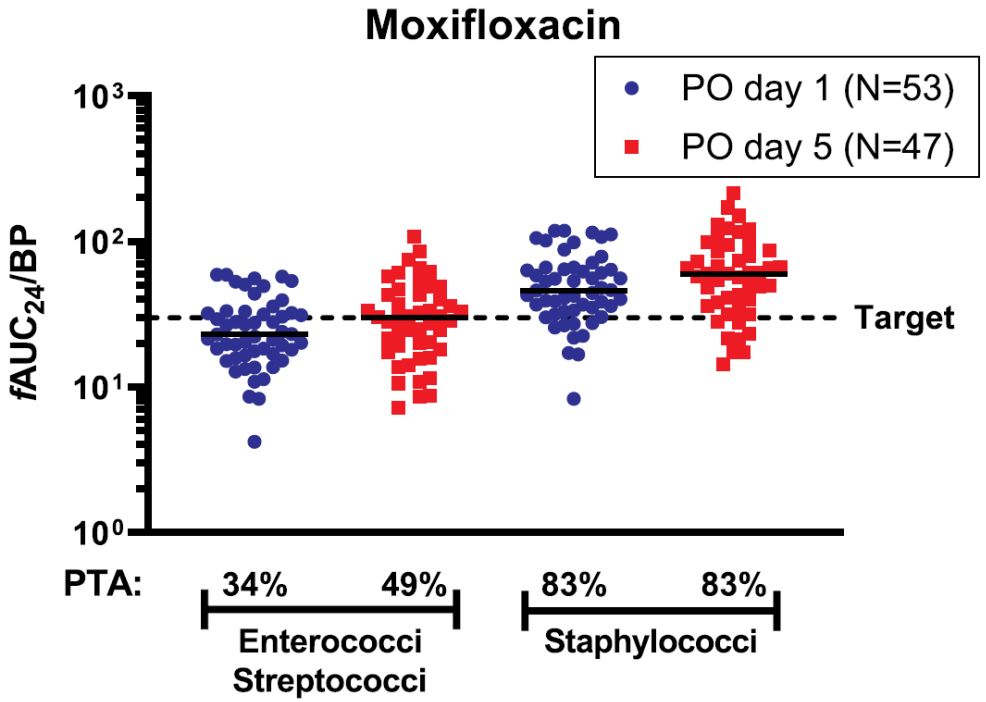

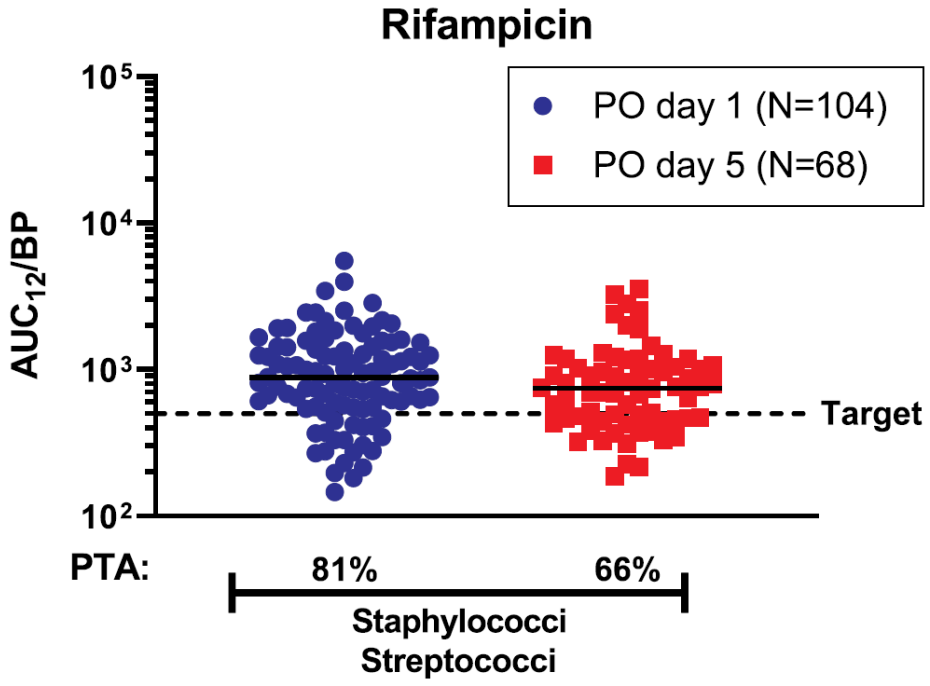

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Clinical Infectious Diseases
MAJOR ARTICLE

Attainment of Target Antibiotic Levels by Oral Treatment of Left-sided Infective Endocarditis: A POET Substudy

Magnus Bock,[1] Anna Marie Theut,[1] Johan G. C. van Hasselt,[2] Hengzhuang Wang,[1,3] Kurt Fuursted,[4] Niels Høiby,[1,3] Christian Johann Lerche,[1,5] Nikolaj Ihlemann,[6] Sabine Gill,[7] Ulrik Christiansen,[8] Hans Linde Nielsen,[9,10] Lars Lemming,[11] Hanne Elming,[12] Jonas A. Povlsen,[13] Niels Eske Bruun,[10,12,14] Dan Høfsten,[15] Emil L. Fosbøl,[15] Lars Køber,[14,15] Martin Schultz,[16] Mia M. Pries-Heje,[15] Jonas Henrik Kristensen,[17,18] Jens Jørgen Christensen,[14,19] Flemming S. Rosenvinge,[20,21] Christian Torp Pedersen,[22,23] Jannik Helweg-Larsen,[24] Niels Tønder,[22] Kasper Iversen,[14,18] Henning Bundgaard,[14,15] and Claus Moser[1,3]

- PK-PD-mäßig (Grenzwert bzw. MHK) eigentlich sehr selten inadäquat bei oraler Verabreichung
  - ✓ Amoxcillin <10% (<<10%) bei Streptokokken

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- PK-PD-mäßig (Grenzwert bzw. MHK) eigentlich nicht adäquat bzw. unzureichend bei oraler Verabreichung
  - Amoxicillin 20% (10%) bei Enterokokken (mindestens !!)
  - Linezolid 30-50% (10%) bei Enterokokken und Staphylokokken
  - Moxifloxacin 30-50% (10%) bei Enterokokken und Staphylokokken
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cave:
wenn man *f*T>MIC >80% fordern würde ….
…. oder *f*T>4xMIC 50% ….

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Zwischenfazit – Oralisierung

- Amoxicillin für Streptokokken (incl. die meisten Pneumokokken) oral adäquat; Daten zur Endokarditis nur mit 4x1 g (TDM dabei notwendig ?); ungeeignet bei ZNS-Infektionen
- Amoxicillin (4x1 g) für Enterokokken und Dicloxacillin (4x1 g) (oder auch Flucloxacillin p.o.) für Staphylokken sehr problematisch; bei Endokarditis auch sonstige Substanzen (POET) wie Moxifloxacin oder Linezolid problematisch
- „Oralisierung“ in Studien
  - meist zugunsten Mehreinsatz von Fluorchinolonen
  - in der Regel nach klinischer Stabilisierung (Subgruppe) und Tage einer initialen parenteralen Therapie !!!

Orale ß-Lactame

	Resorption/Bioverfügbarkeit
Amoxicillin	70-80%
Clavulansäure	~60%
Phenoxymethyl-Pen	~60%
Flucloxacillin	50-60%
Cefalexin/Cefadroxil	80-90%
Cefpodoxim	~50%
Cefixim	~40%
Ceftibuten*	>70%

*evtl. Neuentwicklung mit neuem ß-Lactamase-Inhibitor

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TABLE 3. *Mean serum antibiotic concentrations for study HL-75-47*

Time (h)	Mean serum antibiotic concn (μg/ml ± SE)		
	Cefadroxil monohydrate (500 mg)	Cephalexin monohydrate (500 mg)	Cephradine (500 mg)
0	0	0	0
0.5	5.61 ± 0.78	14.0 ± 2.2	11.3 ± 2.1
1	14.9 ± 1.7	17.9 ± 1.3	15.2 ± 1.3
1.5	15.0 ± 1.1	10.7 ± 1.1	10.6 ± 1.0
2	12.5 ± 0.8	6.02 ± 0.66	6.33 ± 0.77
4	4.63 ± 0.33	1.05 ± 0.16	0.96 ± 0.13
6	1.84 ± 0.14	0.10 ± 0.04	0.13 ± 0.04
8	0.65 ± 0.07	<0.04	<0.04
12	0.11 ± 0.03	<0.04	<0.04

Pfeffer et al *AAC* 1977

Orale Staphylokokken-Betalaktame ?

- Cefalexin
  - MHK 1-2
  - orale Bioverfügbarkeit 80%
  - T ½ 1 h
- Cefadroxil
  - MHK 2-4
  - orale Bioverfügbarkeit 90%
  - T ½ 1.5 h

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Cefalexin 3-4 x 1 g

Cefadroxil 2-3 x 1 g

Pfeffer et al *AAC* 1977

Zusammenfassung/Fazit – Oralisierung

- Teil des Deeskalations-Portfolios, inzwischen heute bei vielen Indikationen (mit RCTs) als „Sequenztherapie“ studiert, viele Studien allerdings mit Fluorchinolonen
- kein Problem bei Substanzen mit guter bis sehr guter oraler Bioverfügbarkeit (und verlässlicher Compliance)
- ß-Lactame bei Streptokokken (Amoxicillin) auch für schwere Infektionen vertretbar; bei Enterokokken und Staphylokokken problematisch; bei Gram-negativer Bakteriämie (unkomplizierte Subgruppe) vertretbar
- Endokarditis: mehr Daten/Erfahrung nötig, keine gute Evidenz für Endokarditis durch Enterokokken oder Staphylokokken (Ausnahme hier: Rifampicin, aber 2x600 mg hier kein Konsens)

Danke fürs Zuhören und Diskutieren